# PMOS EXHIBIT 2

## EXHIBIT 7 OF RYAN DIETZ'S DECEMBER 6, 2018 DEPOSITION: PLAINTIFF'S LAB NOTEBOOK PAGES

Dietz
EXHIBIT NO. 7
MCL 12/4/18

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BOOK PAGE

TITLE/TITRE/TITEL iPS Project

PROJECT/PROJET/PROJEKT

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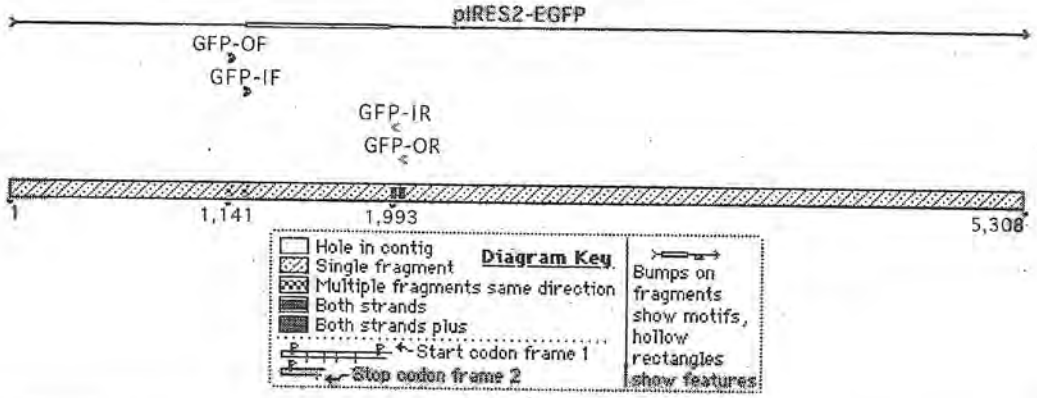
I'm planning a project to see if sustained transient transfection of Yamanaka factor T7 transcripts can induce iPS in MSC or perhaps MEF cultures. I've designed nested primers to make T7 templates for runoff transcription for the four 4 factors + eGFP from an IRES2-eGFP Clontech plasmid Raigove me. Also, I've designed Q primers targeting the 3'UTR of the endogenous transcripts for the 4 factors, so we can monitor if the pluripotency circuit is activated during or after transfection. I envision changing the media for the cells every day, using media spiked with the T7 RNA cocktail, and perhaps collecting cells for QC analysis every ~3 days at passage. Mirus TransIT or IDT Transfectin look like the best bets for the

| | |
|---|---|
| GFP-IF | TAATACGACTCACTATAGGGTTTCTTTGAAAAACACGATGA |
| GFP-IR | CAAATGTGGTATGGCTGATTATG |
| GFP-OF | TCGGTGCACATGCTTTACAT |
| GFP-OR | GGGAGGTGTGGGAGGTTTT |
| KLF-IF | TAATACGACTCACTATAGGGATTAATGAGGCAGCCACCTG |
| KLF-IR | TGTGGGTCACATCCACTACG |
| KLF-OF | GGCTCAGGTACCCCTCTCTC |
| KLF-OR | CTCGTGGGAAGACAGTGTGA |
| KLF-QF | ATGCCCGGACTTACAAAATG |
| KLF-QR | CCCCCAAGCTCACTGATTTA |
| MYC-IF | TAATACGACTCACTATAGGGAGAGCTCCTCGAGCTGTTTG |
| MYC-IR | TCCAGCTCCTCCTCGAGTTA |
| MYC-OF | GGACAGTGTTCTCTGCCTCTG |
| MYC-OR | AATTCCAGCGCATCAGTTCT |
| MYC-QF | GCATGCTCAAAGCCTAACCT |
| MYC-QR | GGCAGTTAAAATTATGGCTGAA |
| OCT-IF | TAATACGACTCACTATAGGGGAGCCGTCTTTCCACCAG |
| OCT-IR | TGTCTACCTCCCTTGCCTTG |
| OCT-OF | GTCCCTAGGTGAGCCGTCTT |
| OCT-OR | CCACCCCTGTTGTGCTTTTA |
| OCT-QF | GGATGGGGAAAGAAGCTCAG |
| OCT-QR | GAACAAAATGATGAGTGACAGACA |
| SOX-IF | TAATACGACTCACTATAGGGACTATTCTCCGCCAGATCTCC |
| SOX-IR | TCTCCAGTTCGCAGTCCAG |
| SOX-OF | GTCTCGAGCTCCGCTTCC |
| SOX-OR | CCCTCCCAATTCCCTTGTAT |
| SOX-QF | TTAACGCAAAAACCGTGATG |
| SOX-QR | AGTCCCCCAAAAAGAAGTCC |



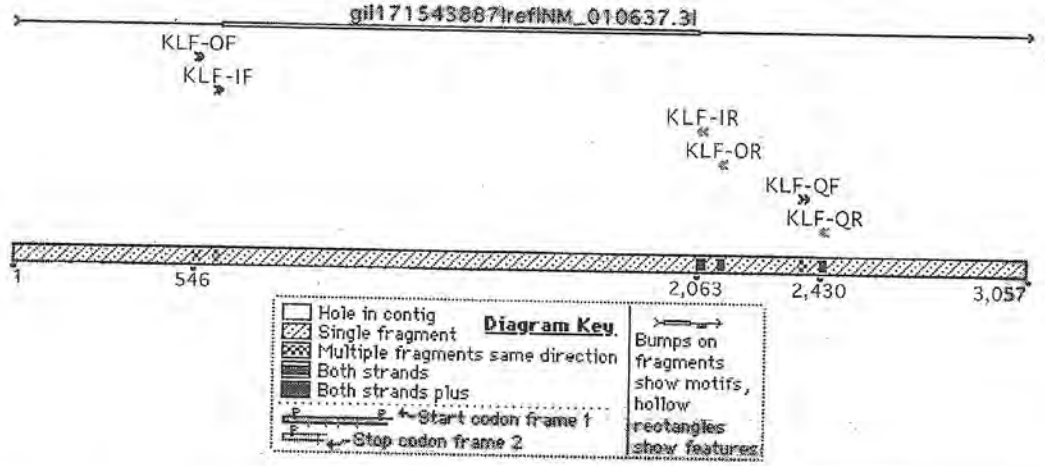




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EXHIBIT 7
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3 -112
BOOK PAGE

TITLE/TITRE/TITEL iPS Project PROJECT/PROJET/PROJEKT

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Discussed iPS project with Derrick and got okay to proceed, as long as expenditures remain modest. Idea is to try and convert MEFs into iPS by repeated transfection of reinprotein factor-encoding synthetic mRNAs over a 10-14 day time course. Plan to PCR up the T7 templates from murine ES RNA using the primers I have already purchased (p.85). I'll use Ambions MESSAGEmachine to make capped, polyadenylated transcript and (most likely) TransIT to facilitate daily transfection be direct administration of RNA + cationic reagent to culture medium. Will use eGFP mRNA to optimize transfection conditions and probably also to monitor transfection efficiency during experiment. Derrick recommends using eGFP RNA at substantially lower concentration than the Y factor RNA in these trials. Also, he said we should definitely go with MEFs for the initial experiment, not MSCs, since they are a known quantity vis-à-vis iPS generation. If we see ES like colonies, we should take them to blastocyst injection immediately to validate pluripotency. For this purpose, we need reporter cells. I will order a ROSA26 (lacZ) mouse (male, breeding age i.e. 10-12 wks) so we can get appropriate MEFs. As soon as mouse arrives, mate to two B6 females. Check for vaginal plugs (signifying pregnancy) and wait 13 days before recovering embryos to make MEFs. ~~Also~~ Will need to check for ROSA26 heterozygozity by β-Gal staining of tissue samples — we only want ROSA26+ MEFs for the experiment. Once embryos are recovered, mate the ROSA26 again to produce replacement animals should this mouse die.

Want to try 5-azadeoxycytidine and Valproic acid as adjuvants to iPS generation in this experiment. Reagents are available from VWR.

Needs:

- Aza deoxycytidine
- Valproic Acid
- MESSAGEmachine Ultra

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7/19/08

TITLE/TITRE/TITEL T+24-8 HRS FACS PROJECT/PROJET/PROJEKT iPS

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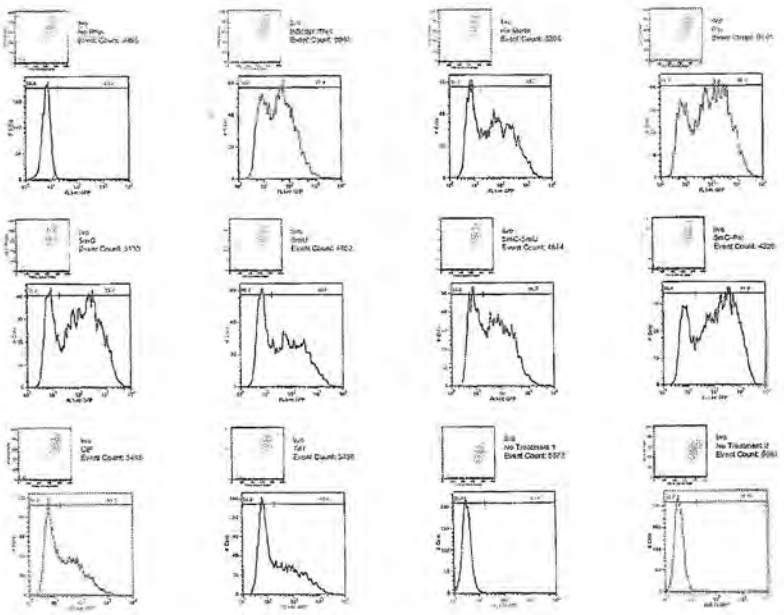

| Sample | Ancestry Subset Value Type For | live Freq. o.. | live GFP+ Freq. o... | live GFP+ Geom. ... FL1-H,... | live GFP+ Mean FL1-H,... | live GFP- Freq. o... | live GFP- Geom. ... FL1-H,... | live GFP- Mean FL1-H,... |
|---|---|---|---|---|---|---|---|---|
| 1: No RNA | | 22.5 | 0.65 | 25.3 | 26 | 99.4 | 6.29 | 6.71 |
| 2: mScript RNA | | 27.8 | 65.1 | 78.2 | 132 | 34.9 | 8.27 | 9.12 |
| 3: No Mods | | 26.3 | 63.7 | 129 | 268 | 36.3 | 7.3 | 8.07 |
| 4: Psi | | 25.7 | 75.1 | 165 | 342 | 24.9 | 7.51 | 8.35 |
| 5: 5mC | | 25.7 | 73.1 | 200 | 428 | 26.9 | 7.64 | 8.35 |
| 6: 5mU | | 24 | 59.7 | 135 | 297 | 40.3 | 7.13 | 7.84 |
| 7: 5mC-5mU | | 24.2 | 61.7 | 99.4 | 182 | 38.3 | 7.45 | 8.27 |
| 8: 5mC-Psi | | 21.6 | 76.6 | 210 | 425 | 23.4 | 7.37 | 8.12 |
| 9: CIP | | 27.3 | 46.2 | 77.6 | 145 | 53.8 | 6.69 | 7.49 |
| 10: TdT | | 27.5 | 46.4 | 105 | 230 | 53.6 | 6.67 | 7.36 |
| 11: No Treatment 1 | | 27.9 | 0.14 | 24.5 | 25.2 | 99.9 | 3.18 | 3.44 |
| 12: No Treatment 2 | | 28.3 | 0.15 | 23.3 | 23.6 | 98.3 | 3.42 | 3.7 |
| Mean | | 25.8 | [illegible] | [illegible] | [illegible] | [illegible] | [illegible] | [illegible] |
| StdDev | | 2.34 | 30 | [illegible] | [illegible] | [illegible] | [illegible] | [illegible] |

5mC-Ψ looks like the winner here, with 5mC & Ψ alone close behind. There hasn't been much of a falloff vs +24 HRS across the board, but 'No Mods' has done a bit worse in this respect than the 5mC/Ψ and mScript wells. (See p.23). I stained with PI, but again haven't fixed to comp here. Settings for PMTs were same as for +24 hrs:

FSC E00 1 Lin FL1 431 Log FL3 650 1 Lin
SSC 350 1 Lin FL2 613 Lin

No treatment cells ran maybe 40% faster than others, suggesting there has been some cell death in treated wells.

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DATE/DATUM 4/29/09

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wells show dose-dependent brightness relationship. Does look like only about half the cells are expressing significant GFP – similar to MEF experience.

T6 plate: Looks good for B18R. Hasn't been too much change since yesterday. In the B18R+ wells only the most aggressively dosed (2-4-8-16) well is close to being trashed, and even that has quite a few small clusters. Cell density in the other B18R+ wells is poor, but not terrible. GFP expression still looks fair, esp in the lower dox wells – maybe a 4 or even better in the 2-2-2, 2-2-4 wells. B18R- wells look terrible – huge numbers of floaters (though there are quite a few in the B18R+ wells too); still a few small islands of cells, but with very feeble GFP expression. Minimal phenoshift now across the whole plate.

Should take ~~cells~~ these cultures to FACS today, if possible.

12:00AM FACSed the BJ plate. By eye, GFP expression looked down by maybe a factor of 2 relative to 6:45 AM check. See p.63 for FACS data.

4:50PM Very faint GFP in B18R+, none in B18R-. Five terminated transfections. Looks like we got ~6 days decent GFP expression in B18R+ wells, ~4 days in B18R- (4.5 perhaps). Lot of toxicity all around, but considerably worse in B18R- wells.

5:30PM Set 4 x 12-well plates of HEKn, ~10K per well, in HEK media (no Matrigel). Added a thawed vial of cells to 3ml media in a 14ml tube, used 1ml syringe to dispense 40µl aliquots. (40µl ÷ (1000µl + 500µl) x $10^6$ = $10^4$ cells.)

FRI 1/30 4:00PM Fed and split BJs from remaining 10 cm plate and 6-well to 2 x 15 cm dishes.

In T6 plate Wells 1-3 show significant central islands, 4 is pretty trashed. All B18R- wells are trashed except one of the 2-2-4 replicates. All wells show more cellularity at the edge of the well. Phenotypes apparent, reminiscent of earlier, late-stage hiPF trials.

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